MAJOR ARTICLE

Changes in *Neisseria meningitidis* Disease Epidemiology in the United States, 1998–2007: Implications for Prevention of Meningococcal Disease

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(See the editorial commentary by Pelton, on pages 192–3.)

Background. In January 2005, a quadrivalent (serogroups A, C , Y, and W-135) meningococcal conjugate vaccine was licensed for use in adolescents. This report describes the epidemiologic features of meningococcal disease in the United States from January 1998 through December 2007, before and during implementation of adolescent quadrivalent meningococcal conjugate vaccination.

Methods. Data were collected from active surveillance for invasive *Neisseria meningitidis* conducted through the Active Bacterial Core surveillance (ABCs) sites during 1998–2007. Isolates from cases were serogrouped at the ABCs site and confirmed at the Centers for Disease Control and Prevention. Estimates of the incidence and number of cases in the 50 states were calculated, standardizing for race and age group.

Results. In the period 1998–2007, a total of 2262 cases of meningococcal disease were reported from ABCs sites; 11.3% of these cases were fatal. The estimated United States average annual incidence of meningococcal disease was 0.53 cases per 100,000 population (95% confidence interval, 0.51–0.55), and an estimated 1525 (95% confidence interval, 1470–1598) cases occurred annually. The annual incidence decreased 64.1%, from 0.92 cases per 100,000 population in 1998 to 0.33 cases per 100,000 population in 2007. Infants aged <1 year have the highest incidence of meningococcal disease (5.38 cases per 100,000 population). After introduction of the quadrivalent meningococcal conjugate vaccine, no significant decrease in serogroup C or Y meningococcal disease was seen among those aged 11–19 years in 2006–2007, compared with 2004–2005.

Conclusions. Before the introduction of the quadrivalent meningococcal conjugate vaccine, the incidence of meningococcal disease in the United States decreased to a historic low. However, meningococcal disease still causes a substantial burden of disease among all age groups. Future vaccination strategies may include targeting infants and preventing serogroup B meningococcal disease.

In January 2005, a quadrivalent (serogroups A, C, Y, and W-135) meningococcal conjugate vaccine (MCV4) was licensed. Serogroups C and Y, as well as serogroup B, which is not contained in this vaccine, cause most meningococcal disease in the United States [1–3]. In May 2005, the Advisory Committee on Immunization Practices recommended MCV4 for routine use in adolescents aged 11–18 years and others aged 2–55 years

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at increased risk for meningococcal disease [4–6]. Although it was recommended that college freshmen be educated to make an informed decision about being vaccinated with meningococcal polysaccharide vaccine in 2000, no recommendation was made for administering the meningococcal polysaccharide vaccine except in high-risk groups [7]. MCV4 was the first meningococcal vaccine recommended for routine use in the United States. By the fall of 2007, coverage among those aged 13–17 years was 32.4% [8]. As of February 2009, there are no licensed vaccines to protect against meningococcal disease in infants aged <2 years or against serogroup B meningococcal disease; however, several vaccine candidates are in development, and infant vaccines against serogroup C meningococcal disease are used in several countries in Europe, Canada, and Australia [9–12].

Patterns in meningococcal disease incidence and serogroup distribution during the past decade will inform future meningococcal disease prevention strategies. This report describes the epidemiologic features of meningococcal disease in the United States from January 1998 through December 2007 before and during implementation of adolescent MCV4 vaccination.

METHODS

Surveillance. Active surveillance for disease caused by *Neisseria meningitidis* is conducted through the Active Bacterial Core surveillance (ABCs) sites. This population- and laboratory-based surveillance system is supported by the Centers for Disease Control and Prevention (CDC) as part of its Emerging Infections Program network (http://www.cdc.gov/ncidod/DBMD/abcs/).

During 1998–2007, the area under surveillance included 3 counties in the San Francisco Bay Region, California, Connecticut, Georgia, Maryland, Minnesota, Oregon, 5 counties in Tennessee, and 15 counties surrounding Albany and Rochester, New York. Beginning in August 1999, a total of 11 counties in Tennessee were included in the surveillance area. In 2000, a total of 5 counties in the Denver, Colorado, metropolitan area were added; New Mexico was the most recent addition in 2004. In 2007, the total population under surveillance was ~39.5 million, or 13% of the United States (US) population.

We defined a case of meningococcal disease as the isolation of *N. meningitidis* from a normally sterile site, such as blood, cerebrospinal fluid, pleural, or joint fluid, from a resident of an ABCs site from 1 January 1998 through 31 December 2007. College students are defined as residents of the surveillance site. A case report form was completed for each case. Periodic laboratory audits were conducted to identify unreported cases.

The following hierarchical definition was used to classify a single syndrome for cases: a patient was defined as having meningitis if a clinical diagnosis of meningitis had been entered into the patient's medical record or if *N. meningitidis* was isolated from cerebrospinal fluid, pneumonia if pneumonia was entered into the patient's medical record and *N. meningitidis* was isolated from blood or pleural fluid, septic arthritis if *N. meningitidis* was isolated from joint fluid, and isolated bacteremia if *N. meningitidis* was isolated from blood and no localizing clinical syndrome was described.

Laboratory methods. Serogrouping of *N. meningitidis* was performed at state public health laboratories, after which the isolates were sent to the CDC, where slide agglutination serogrouping and serogroup-specific real-time polymerase chain reaction (PCR) were performed [13]. If the CDC slide agglutination or PCR testing confirmed the state serogroup result, that result was used as the final serogroup. If the CDC slide agglutination and PCR both differed from the state serogroup, the CDC result was used as the final serogroup. If an isolate was nonviable or contaminated on arrival at the CDC after sending 2 times, the result from the state laboratory was used.

Multilocus sequence typing (MLST) was performed at the CDC and the University of Pittsburgh on all isolates from cases occurring during 2000–2005. Chromosomal DNA was extracted by streaking 1–2 colonies onto sheep blood agar or chocolate agar, incubating at 37°C overnight, placing a thick suspension in 0.5 mL of phosphate-buffered saline or Tris hydrochloride (pH, 8), and boiling for 20 min. MLST was performed as described elsewhere [14, 15]. DNA sequences were determined using both the forward and reverse strands.

Statistical analyses. Incidence rates were calculated using US Census data for the ABCs sites, and estimates of the number of cases and deaths in the 50 states were calculated, standardizing for race and age group. For rate calculations, an ABCs site was included only if data were collected for the complete year. Oregon has reported higher rates of serogroup B and overall meningococcal disease because of hyperendemic serogroup B disease that was first reported in 1994 [16, 17]. We verified that the Oregon clonal outbreak was not consistent with disease patterns in other states by comparing disease incidence in Oregon to the 50 states using reports from the National Notifiable Diseases Surveillance System (NNDSS). During 1995–2005, Oregon reported a meningococcal disease incidence of 2.36 through the NNDSS. The other 49 states reported incidence of 0.53–1.36 cases per 100,000 population (CDC, unpublished data). Accordingly, incidence was standardized by race and age group to the US population using incidence excluding Oregon. The confidence interval (CI) around the standardized rate was calculated using a method derived from the relationship between the Poisson distribution and the gamma distribution [18]. Cases in Oregon were then added back in for the final standardized incidence rate and estimated annual burden of disease in the United States. For all other analyses, data are presented including cases from Oregon unless otherwise noted. Incidence rates are reported as cases per 100,000 population.

Table 1. Active Bacterial Core Surveillance (ABCs) Number of Cases, Rates, and Annual Estimated United States (US) Incidence Rates of Meningococcal Disease, 1998–2007

Characteristic	No (%) of ABCs cases (includes OR)	ABCs incidence (excludes OR)	Annual US incidence (95% CI)
Age group, years			
<1	299 (13)	5.22	5.38 (4.73–6.10)
1–4	276 (12)	0.96	1.04 (0.90–1.20)
5–14	250 (11)	0.38	0.38 (0.32–0.43)
15–24	471 (21)	0.77	0.78 (0.70–0.86)
25–64	641 (28)	0.30	0.28 (0.26–0.31)
⩾65	325 (14)	0.68	0.69 (0.61–0.78)
Sex			
Male	1170 (52)	0.52	0.56 (0.51–0.59)
Female	1092 (48)	0.49	0.51 (0.48–0.54)
Race			
White	1494 (66)	0.42	0.50 (0.48–0.54)
Black	419 (19)	0.66	0.73 (0.66–0.80)
Other	101 (4)	0.29	0.44 (0.27–0.44)
Unknown	248 (11)	…	…

NOTE. Incidence standardized by race and age group to the population of the 49 US states using incidence from Active Bacterial Core surveillance, excluding Oregon. Cases in Oregon were added back for the final standardized incidence rate. CI, confidence interval; OR, odds ratio.

Multivariable logistic regression analysis with the SAS software system, version 9.1 (SAS Institute), was used to determine independent risk factors for a fatal case. Two-way interactions and colinearity were assessed in the model.

RESULTS

In the years 1998–2007, a total of 2262 cases of meningococcal disease were reported from ABCs sites, resulting in an estimated US average annual incidence of 0.53 cases per 100,000 population (95% CI, 0.51–0.55); 11.3% of these cases were fatal. The annual incidence decreased 64.1%, from 0.92 per 100,000 population in 1998 to 0.33 per 100,000 population in 2007. The incidence of meningococcal disease varied by season, with more cases occurring during January and February (12% each) and the fewest cases occurring during August (5%). The incidence of meningococcal disease ranged from 0.43 cases per 100,000 population to 1.52 cases per 100,000 population (median, 0.57) among sites in the ABCs network. The incidence was highest in Oregon (1.52 cases per 100,000 population), compared with the other ABCs sites combined (0.52 cases per 100,000 population); the incidence of serogroup B–specific meningococcal disease was 1.01 cases per 100,000 population in Oregon, compared with 0.15 cases per 100,000 population in the other surveillance sites. In 1998, the incidence of serogroup B meningococcal disease in Oregon was 1.40 cases per 100,000 population, compared with 0.16 cases per 100,000 population in the 7 other existing surveillance sites; in 2007, incidence decreased to 0.43 cases per 100,000 population in Oregon and 0.08 cases per 100,000 population in the 9 other surveillance sites.

Date of birth was available for all cases; 299 cases (13%) occurred in children aged 0–12 months, compared with 276 (12%) in children aged 1–4 years, 250 (11%) in persons aged 5–14 years, 471 (21%) in persons aged 15–24 years, 641 (28%) in persons aged 25–64 years, and 325 (14.4%) in persons aged ⩾65 years. Male patients accounted for 51.7% of cases. Female patients were significantly older than male patients (median age, 25 years in female patients, compared with 17 years in male patients; $P < .001$). Overall incidence did not differ by sex, but among persons aged ⩾65 years, female patients had a higher incidence of disease than male patients, and conversely, among persons aged <5 years, male patients had a higher incidence than female patients (Table 1 and Table 2). The incidence of meningococcal disease among black persons was 0.72 cases per 100,000 population (95% CI, 0.66–0.80), compared with 0.50 cases per 100,000 population (95% CI, 0.48–0.54) among white persons and 0.44 cases per 100,000 population (95% CI, 0.27–0.44) among other race categories combined (Table 1). Differences in the incidence of meningococcal disease by race diminished during the study period (Figure 1).

N. meningitidis was isolated from blood in 1726 cases (78.6%), from cerebrospinal fluid in 690 cases (32.8%), and from joint fluid in 35 cases (1.7%). In 184 cases (8.1%), *N. meningitidis* was isolated from both the blood and cerebrospinal fluid. Information on syndrome was available for 2220 cases (98.1%). Meningitis was the most frequent clinical syndrome,

Table 2. Annual Estimated United States Incidence Rates (per 100,000 Population) of Meningococcal Disease by Age Group, Race, And Sex, 1998–2007

	Incidence Rate per 100,000 Population (95% CI)					
	Male patients			Female patients		
Age group, years	White	Black	Other	White	Black	Other
<1	6.7 (5.54–8.04)	6.97 (4.93–9.57)	2.70 (0.74–6.93)	4.71 (3.72–5.89)	2.28 (1.18–3.99)	2.91 (0.86–7.33)
1–4	1.35 (1.10–1.66)	0.64 (0.35–1.08)	2.01 (1.06–3.52)	0.84 (0.49–1.34)	0.84 (0.49–1.34)	0.00 (0.00–0.66)
5–14	0.33 (0.26–0.42)	0.50 (0.33–0.71)	0.64 (0.30–1.12)	0.31 (0.23–0.40)	0.66 (0.46–0.90)	0.37 (0.13–0.75)
15–24	0.75 (0.64–0.89)	1.25 (0.96–1.58)	0.70 (0.25–1.01)	0.80 (0.67–0.94)	0.63 (0.45–0.89(	0.29 (0.05–0.52)
25–64	0.25 (0.22–0.30)	0.74 (0.62–0.90)	0.12 (0.10–0.48)	0.24 (0.21–0.29)	0.40 (0.34–0.50)	0.11 (0.05–0.22)
⩾65	0.38 (0.29–0.50)	0.43 (0.17–0.79)	0.75 (0.24–1.54)	0.90 (0.78–1.05)	0.78 (0.49–1.15)	0.79 (0.32–1.47)

NOTE. Incidence standardized by race and age group to the population of the 49 US states using incidence from Active Bacterial Core surveillance, excluding Oregon. Cases in Oregon were added back for the final standardized incidence rate.

reported in 1115 cases (50.2%), followed by bacteremia in 832 (37.5%), pneumonia in 204 (9.2%), and septic arthritis in 45 (2.0%). The median age of patients with pneumonia was higher than that of patients with meningitis or bacteremia (68.5 vs 18 years; $P \leqslant .001$). Ninety-two percent of patients were hospitalized; the median number of days hospitalized was 6 days (range, 0–195 days). Patients with bacteremia were hospitalized for a median of 5 days, patients with pneumonia were hospitalized for a median of 6 days, and patients with meningitis were hospitalized for a median of 7 days. Of the 178 patients who were not hospitalized (8%), 26% died.

Isolates were available for serogrouping at the CDC or the state health department for 2103 cases (93%). Of the 1846 isolates tested at both the state laboratory and the CDC, 88 (4.8%) had discrepant results between the 2 laboratories; of these, 36 (40.9%) were not able to be grouped at the state laboratory but were determined to be serogroup B at the CDC. Including Oregon, serogroup C accounted for 525 (25.0%), serogroup B for 821 (39.0%), serogroup Y for 633 (30.0%), W-135 for 51 (2.4%), and organisms not able to be grouped for 66 (3.1%) isolates. Excluding Oregon, serogroup C accounted for 454 (28.8%), serogroup B for 471 (29.9%), serogroup Y for 548 (34.8%), W-135 for 40 (2.5%), and organisms not able to be grouped for 57 (3.6%) isolates. Serogroups A, X, and Z accounted for 1, 2, and 4 isolates, respectively, and none of these isolates were from Oregon. The median age of patients was 12 years for those with serogroup B, 20 years for those with serogroup C, 40 years for those with serogroup Y, and 53 years for those with serogroup W-135. Figure 2 shows the proportion of cases by serogroup that caused meningitis, bacteremia, and pneumonia.

Of the 275 serogroup C isolates for which MLST was performed (for the period 2000–2005), 210 were sequence type (ST) 11/electrophoretic type (ET) 37 clonal complex (CC), 20 were ST-103, and 13 were ST-32/ET-5 CC. There were 8 additional STs for which there were ⩽10 serogroup C isolates during 2000–2005. Of the 312 serogroup Y isolates with MLST performed, 291 were ST-23/A3 CC, 15 were ST-167, and the remaining 6 isolates were spread among 4 STs. Of the 513 serogroup B isolates, 251 were the ST-32/ET-5 CC circulating in Oregon; 156 (62%) of these isolates were from Oregon. Among other serogroup B isolates, 130 were ST-41/44 CC, and 32 were ST-162. There were an additional 15 serogroup B STs each with ⩽21 isolates.

Estimated annual burden of meningococcal disease. An estimated 1525 (95% CI, 1470–1598) cases of meningococcal disease occurred annually in the United States during this period, with an estimated 2498 cases in 1998 and 1005 cases in 2007. Table 3 gives the standardized incidence and annual estimated national burden of disease and deaths associated with meningococcal disease by age group and serogroup during 1998–2007. Infants aged <1 year had the highest rates of meningococcal disease (5.38 cases per 100,000 population). Among infants aged <1 year, the greatest number of cases by month of age occurred in infants aged 2–3 months (21.9%), who had an estimated incidence of 7.1 cases per 100,000 population (Table 3). Serogroup B meningococcal disease peaked among infants aged 0–3 months, serogroup C meningococcal disease peaked among those aged 4–5 months, and serogroup Y meningococcal disease was elevated in those aged 0–7 months. After the first 5 years of life, there was a second peak in the incidence of meningococcal dis-

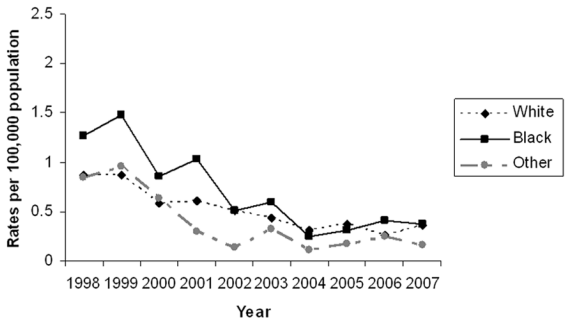

Figure 1. Trends in meningococcal disease incidence by race, 1998–2007.

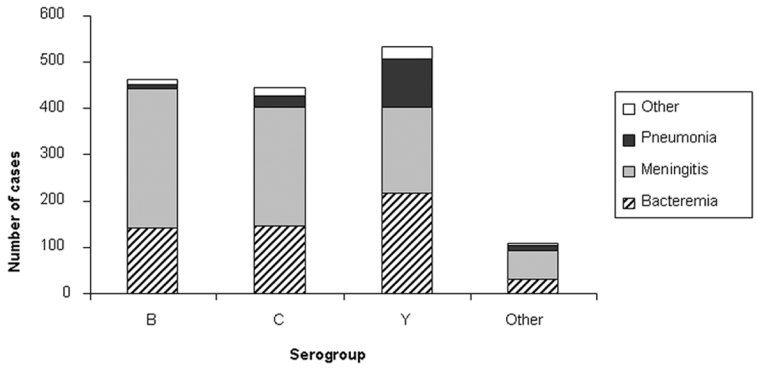

Figure 2. Number of cases of meningococcal disease causing meningitis, pneumonia, or bacteremia, by serogroup, Active Bacterial Core surveillance sites (excluding cases from Oregon), 1998–2007. Other includes serogroups A, W-135, X, and Z, as well as organisms that were not able to be grouped.

ease among adolescents aged 14–17 years and those aged 18–24 years.

Risk of death and meningococcal disease. Case-fatality ratios were highest among persons aged ⩾65 years (23.2%) and decreased with lower age (Table 3). Isolated bacteremia and meningococcal pneumonia had higher case-fatality ratios (13.2% and 15.9%, respectively) than meningococcal meningitis (9.0%). The case-fatality ratio was highest among cases caused by serogroup W-135 (16.3%) and lower among cases caused by serogroup B strains (8.8%). Excluding cases from Oregon, the case-fatality ratio caused by serogroup B strains increases to 11.2%. In a multivariable model including serogroup, isolate source, syndrome, age group, race, and surveillance site, patients who had meningitis were less likely to die than patients with isolated bacteremia (odds ratio [OR], 0.65; 95% CI, 0.46–0.92). Compared with infants aged <1 year, patients who died were more likely to be aged 20–34 years (OR, 2.04; 95% CI, 1.03–4.03), 35–64 years (OR, 2.67; 95% CI, 1.41–5.06), or ⩾65 years (OR, 4.26;

Table 3. Annual Estimated National Burden of Disease, Standardized Incidence (per 100,000 Population), and Annual Estimated Number of Deaths and Case-Fatality Ratios (CFRs) Associated with Meningococcal Disease by Age Group and Serogroup, United States, 1998–2007

	Serogroup B		Serogroup C		Serogroup Y		Total[a]	
Age group	No of cases (incidence)	No of deaths (CFR)	No of cases (incidence)	No of deaths (CFR)	No of cases (incidence)	No of deaths (CFR)	No of cases (incidence)	No of deaths (CFR)
<1 year	123 (3.08)	10	21 (0.53)	3	60 (1.50)	1	215 (5.38)	13 (6.0)
0–1 month	27 (4.05)	…	2 (0.29)	…	14 (2.14)	…	46 (6.92)	3 (6.5)
2–3 months	27 (4.05)	…	2 (0.29)	…	13 (2.00)	…	47 (7.08)	3 (6.5)
4–5 months	23 (3.45)	…	8 (1.14)	…	14 (2.14)	…	46 (6.88)	2 (4.3)
6–7 months	25 (3.75)	…	4 (0.57)	…	11 (1.71)	…	42 (6.33)	3 (7.1)
8–9 months	12 (1.80)	…	3 (0.43)	…	3 (0.43)	…	18 (2.66)	1 (5.5)
10–11 months	9 (1.35)	…	3 (0.43)	…	4 (0.57)	…	16 (2.35)	1 (6.2)
1 year	29 (0.74)	0	11 (0.27)	2	12 (0.31)	0	59 (1.47)	2 (3.4)
2–4 years	45 (0.39)	2	35 (0.29)	2	14 (0.12)	1	105 (0.90)	5 (4.8)
5–9 years	30 (0.15)	5	35 (0.18)	2	13 (0.06)	3	83 (0.42)	10 (12.0)
10–13 years	12 (0.07)	1	20 (0.12)	2	15 (0.09)	1	49 (0.30)	4 (8.2)
14–17 years	23 (0.14)	1	45 (0.27)	6	48 (0.29)	3	124 (0.74)	12 (9.7)
18–24 years	75 (0.27)	9	85 (0.30)	14	42 (0.15)	2	213 (0.76)	29 (13.6)
25–64 years	105 (0.07)	10	122 (0.08)	16	171 (0.11)	25	429 (0.28)	55 (12.8)
⩾65 years	29 (0.08)	12	48 (0.13)	15	149 (0.42)	27	248 (0.69)	59 (23.8)
Total	471 (0.16)	50 (10.6)	422 (0.15)	62 (14.7)	524 (0.18)	63 (12.0)	1525 (0.53)	189 (12.4)

NOTE. Incidence standardized by race and age group to the population of the 49 US states using incidence from Active Bacterial Core surveillance, excluding Oregon. Cases in Oregon were added back for the final standardized incidence rate.

[a] Total cases, incidence, and deaths include serogroup W-135 and other serogroups. National estimates of these serogroups cannot be performed because of the small numbers.

Table 4. Incidence (per 100,000 Population) of Meningococcal Disease by Age and Serogroup, 1998–2007

	Serogroup C, Y, and W-135 cases per 100,000 population (95% CI)			Serogroup B cases per 100,000 population (95% CI)		
Year	Aged <1 year	Aged 11–19 years	Aged ⩾20 years	Aged <1 year	Aged 11–19 years	Aged ⩾20 years
1998–1999	5.69 (4.13–7.63)	1.10 (0.87–1.37))	0.48 (0.42–0.56)	3.30 (2.19–4.81)	0.23 (0.14–0.36)	0.14 (0.10–0.18)
2000–2001	2.53 (1.60–3.82)	0.67 (0.50–0.87)	0.39 (0.33–0.45)	3.67 (2.54–5.15)	0.24 (0.15–0.37)	0.12 (0.09–0.16)
2002–2003	1.84 (1.08–2.93)	0.47 (0.34–0.64)	0.22 (0.18–0.27)	3.86 (2.73–5.32)	0.18 (0.10–0.29)	0.10 (0.08–0.13)
2004–2005	0.63 (0.25–1.33)	0.23 (0.15–0.35)	0.16 (0.13–0.20)	2.59 (1.71–3.77)	0.10 (0.05–0.19)	0.06 (0.04–0.09)
2006–2007	1.07 (0.53–1.91)	0.27 (0.18–0.40)	0.22 (0.18–0.26)	1.79 (1.08–2.81)	0.04 (0.01–0.10)	0.05 (0.04–0.08)

NOTE. Incidence standardized by race and age group to the population of the 49 US states using incidence from Active Bacterial Core surveillance, excluding Oregon. Cases in Oregon were added back for the final standardized incidence rate. CI, confidence interval.

95% CI, 2.16, 8.43). Serogroup, isolate source, and race were not independently associated with a fatal outcome. The overall case-fatality ratio did not change significantly during the 10-year period (data not shown).

Trends in meningococcal disease among those aged 11–19 years. During 1998–2007, the rate of meningococcal disease decreased among those aged 11–19 years for serogroups contained in MCV4 (C, Y, and W-135) and for serogroup B, which is not in MCV4. The rate of serogroup C, Y, and W-135 disease did not significantly differ between 2004–2005 and 2006–2007. The rate of serogroup B meningococcal disease did not significantly decrease during 2006–2007, compared with 2004–2005 (Table 4).

DISCUSSION

Rates of meningococcal disease in the United States in 2007 were at a historic low [2]. The annual incidence was one-half the lowest previously observed rate of 0.6 cases per 100,000 population, seen in the early 1970s [19]. Meningococcal disease has a cyclical nature, with peaks and troughs occurring in a 5-to-8–year pattern; however, the disease pattern of the past 10 years is outside the previously observed periodicity of disease [1, 2]. The increased incidence of meningococcal disease in Oregon during this period due to the clonal outbreak of serogroup B disease also decreased. There is historical precedence for major shifts in meningococcal disease patterns; large serogroup A outbreaks occurred in the United States in the first part of the 20th century, but by the 1950s serogroup A meningococcal disease outbreaks disappeared in the United States and other industrialized countries [1, 19].

It is likely that a combination of environmental, organism, and host factors is responsible for this remarkable decrease in the incidence of meningococcal disease. Environmental risk factors, such as smoking and crowding, have been shown to be risk factors for meningococcal disease, and changes in these factors may have contributed to the decrease in meningococcal disease rates [20–22]. Other studies have indicated race as a marker of other risk factors for disease, such as low socioeconomic status and crowding [23]. The decrease in racial disparities observed may also be attributable to changing dynamics of environmental risk factors, such as crowding. A study performed in Maryland observed that the increased incidence of serogroup C and serogroup Y meningococcal disease in the 1990s was associated with the emergence of new antigenic variants of *N. meningitidis* [24]. Population immunity to these circulating strains was likely high after the peak of disease observed in the 1990s and may contribute to decreased transmission of *N. meningitidis*. In addition, vaccination with 7-valent pneumococcal conjugate vaccine and widespread use of fluoroquinolone antibiotics may be changing the dynamics of organisms carried in the nasopharynx [25, 26]. Although we are unable to provide a good explanation for the sharp decrease in disease incidence, this decrease occurred before implementation of adolescent vaccination with MCV4.

We did not observe any effect of MCV4 on meningococcal disease rates in 2006–2007, early after the introduction of MCV4, compared with 2004–2005. Serogroup B disease among those aged 11–19 years also decreased during this period, suggesting that multiple factors contributed to the observed decrease in meningococcal disease. Lack of an effect from MCV4 introduction is not surprising given vaccine uptake in the early years; coverage among adolescents aged 13–17 years was estimated to be 11.4% in 2006, increasing to 32.4% in 2007 [8]. These early data do not imply that MCV4 will not affect disease; continued disease surveillance and vaccine effectiveness studies will provide an important measure of MCV4 impact.

Even with the observed recent historic low rate of meningococcal disease, it continues to cause considerable morbidity and mortality each year in the United States. Serogroup B was the most common serogroup during 2002–2006, but in 2007 serogroup Y was the most common serogroup. Compared with the mid-1990s, when the proportion of serogroup Y cases increased from 2% during 1989–1991 to 32.6% in 1996, the proportion of serogroup Y disease has decreased, although serogroup Y still caused 26% of meningococcal disease cases in 2007 [2, 27]. Serogroup Y causes most of the meningococcal

pneumonia cases among older adults, but our data also highlight the large proportion of disease caused by serogroup Y among infants aged <6 months. In addition, case-fatality ratios did not decrease during this period. The 10%-14% case-fatality ratio among adolescents highlights the importance of vaccination strategies to prevent development of disease.

Our surveillance system only captures cases of meningococcal disease when *N. meningitidis* is recovered from a normally sterile body site. In contrast, the NNDSS is a passive surveillance system that includes probable cases. The average annual rate of confirmed and probable meningococcal disease reported to the NNDSS during 1998–2007 was 10% higher (0.63 cases per 100,000 population) than the rate we observed (CDC, unpublished data). The ABCs is more specific than the NNDSS but likely underestimates the burden of meningococcal disease in the United States.

This report highlights several important aspects of current meningococcal vaccination policy in the United States. Rates of meningococcal disease are highest in infants and toddlers aged <2 years; 50% of these cases are caused by serogroup B, and approximately two-thirds of meningococcal disease in the first year of life occurs in infants aged <6 months, consistent with previous US reports [2, 27, 28]. Quadrivalent (A, C, Y, W-135) and bivalent (C, Y) meningococcal conjugate vaccines are in phase 3 immunogenicity trials in this younger age group, but these vaccines may not produce a robust immune response until after the second or third dose (at 4–6 months of life) [9, 10]. Serogroup B meningococcal vaccines, currently not licensed in the United States, are in phase 2 clinical trials in adolescents and eventually may be targeted in infants [11, 12].

Even though the rate of meningococcal disease is at a historic low in the United States, the next several years will be a critical time for meningococcal disease control in the United States as opportunities for protection through vaccination expand. Recent emergence of ciprofloxacin-resistant *N. meningitidis* strains detected in several states underscores that routine vaccination is a critical prevention tool [29]. As MCV4 coverage increases and new vaccines are introduced, data obtained from active, population-based surveillance will be used to evaluate vaccine effectiveness by detecting breakthroughs and to monitor changes in serogroup distribution, development of antimicrobial resistance, and emergence of new meningococcal strains.

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